FERTILITY IN WOMEN

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FERTILITY IN WOMEN
(A Survey of Data from the last 10 Years' Experience with A.I.D.)

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Artificial insemination with donated semen, though primarily designed to compensate for male sterility, has incidentally yielded information relating to female fertility. This by-product of A.I.D. springs from two aspects of the method. Firstly, semen selected for A.I.D. is characterized by high fertility manifested on the one hand by the density of the spermatozoa (more than 60 millions per ml.), their high viability and invasive capacity, and on the other hand by the absence of stigmata of sub-fecundity such as excessive exfoliation of testicular cells and a high frequency of morphologically abnormal spermatozoa. That these criteria are on the whole adequate is borne out by the rapidity with which conception does occur in a high percentage of women receiving A.I.D. with such semen. The use of fertile semen thus eliminates for all practical purposes the effect of variations in the male factor, and given certain precautions such as the correct planning and management of each case, variations in conception rate reflect female factors.

Secondly, variations in female fertility thus assessed have a significance transcending their immediate clinical importance. The cases presenting themselves for A.I.D. are selected almost entirely by the criterion of male sterility, and thus the women concerned represent an almost random sample of nulligravidae of similar age, group and social status. The randomization attained by selecting women on the basis of male deficiency is of course not perfect, since few cases of very severe and obvious female infertility are referred by the physician for A.I.D. If we estimate the frequency of female infertility by conception rate and other indices of fertility, this estimate will relate to the incidence of female fecundity in corresponding age and social groups; although it will tend to err on the low side because of the exclusion of the most severe and obvious cases of female infecundity.

With this in mind, I have reviewed my experience with about 600 cases presenting themselves for A.I.D. during the last ten years. The analysis has taken into account all cases seen between 1944 and 1954 excepting 150 women who either abandoned treatment or never underwent it, or were lost sight of after conception had occurred. For some purposes the analysis of the data has been limited to random samples of the total rds, numbering 90 to 100 cases each.

TABLE I

		Year Group		
		Before 1950	*1950 onwards*	*All women combined*
Mean age		30.3	30.3	30.3
		%	%	%
No stigmata		25.9	23.8	25
Hypoplasia	Subfertile	10.3	11.9	11
Fibroids	Subfertile	3.4	4.8	4
Retroversion	Subfertile	8.6	21.4	14
Endometrial disorders	Subfertile	5.2	Nil	3
Tubal disorders	Subfertile	15.5	14.3	15
Ovarian disorders	Subfertile	12.0	7.1	10
Menstrual disorders including anovulation	Subfertile	8.6	7.1	8
Pelvic infection	Subfertile	20.7	16.6	19
Cervical dysfunction	Subfertile	55.2	28.6	44
Unspecific stigmata	Subfertile	17.2	23.8	20

The first set of observations to which I want to refer is summarized in Table I. Every woman presenting herself for A.I.D. is subjected to a range of examinations designed to assess female fertility, and thus to minimize waste of time and disappointment. The examination includes a general medical examination as well as the usual series of specific fertility tests, such as hysterosalpingogram or insufflation, or both, endometrial biopsy, invasion test on the cervical mucus, and bacteriological examinations where necessary. The records of this preliminary examination show a high incidence of relatively severe infertility factors in these women, who as a rule take it for granted that they are fertile, having discovered that their husbands might bear the sole responsibility for childlessness.

Table I relates to the frequency with which specific and unspecific stigmata were recorded in two samples of women totalling 100 applying for A.I.D., the first sample covering the period from 1944-50, the second the period from 1950-54. Only relatively severe infertility factors have been taken into account. Thus under pelvic infection I have included only cases in which undoubted symptoms of inflammatory conditions of the adnexa were present. Again, the menstrual disorders taken into account included only severe disorders such as marked irregularity of menstruation or frequent anovulatory cycles. The heading 'Tubal Disorders' relates to occluded tubes. Under the heading 'Ovarian Disorder' cystic conditions and ovarian tumours are included. Fibroids were only recorded as infertility factors if either their size or their site could reasonably be regarded as obstructive in a functional or a topical sense. Retroversion is not commonly regarded as an infertility factor, but has been included in view of the success sometimes achieved by correction of uterine position after all previous

attempts to secure conception have failed. Under 'Unspecific Stigmata' are placed severe systemic disorders such as chronic infections of the urinary tract, pulmonary tuberculosis and unrelenting furunculosis.

It will be seen that in 75% of the subjects the initial examination revealed infertility factors which would render conception unlikely, inadvisable, or impossible. In most cases more than one stigma was discovered so that the prognosis did not rest upon a single defect. The most common infertility factor consisted in impaired cervical function which prevented cervical invasion by spermatozoa or caused their rapid inactivation after invasion of the cervical mucus. Pelvic infection was also prevalent. Endometrial disorders, including tuberculous endometritis were rather less frequently encountered than one would expect from recent hospital experience. The frequency of tubal disorders would have been much higher if minor impairment of tubal function had been included.

The relative frequency of the different infertility factors is of less interest than their combined action which results in only one-quarter of the subjects justifying the application of A.I.D. without preliminary treatment. It might be suggested that this high incidence of infecundity reflects the age of the subjects, their mean age being relatively high (30.3 years). But analysis of the combined data shows that 30% of the 59 women aged 30 years or more were free of infertility signs, whereas the corresponding figure in the 41 under thirties was but 17%. Similar frequences were found in other sample groups. Nor is this relative prevalence of demonstrable infertility a feature of a particular period such as the end of the war or the early post-war period, since the sample groups of the cases investigated between 1944 and 1950 and 1950-54 respectively show no significant difference.

Donated inseminations were never started unless and until there appeared to be a reasonable chance of conception; and this inevitably involved preliminary treatment in the subfertile but 'treatable' subjects. The ultimate fertility of the subjects may be assessed by the conception rate, though the latter is to some extent affected by incidental factors — for instance, persistence by the doctor and perseverance by the patient. No arbitrary limit was set to the number of cycles in which insemination was carried out provided the patient retained her apparent capacity to conceive. In several women A.I.D. was continued for up to 24 cycles, in others it was abandoned after a few attempts; and for the purpose of the present review only those cases are considered who were treated for at least 5 cycles if necessary. With this proviso the conception rate is found to be 57.6% in a sample of 66 cases seen during one year (1951/2). In a more recent series (24 cases) the corresponding rate was 54%. The mean number of cycles under treatment in the above positive cases was 4.3. Dividing the sample groups under discussion into under thirties

and over thirties respectively, no difference whatever in the final conception rate was found (57.6% in each age group). But it may be of interest that the younger women required more inseminations than the older ones, viz. 5.3 cycles in the under thirties as against 3.2 cycles in the over thirties. This difference may have some relation to the observation mentioned above that the initial incidence of subfertility was higher in the under thirties. It would appear, therefore, that the younger women compensate for their initial disadvantage by relatively good response to treatment.

The conception rate was also calculated for a sample of 19 women aged 35 or over, and in these the conception rate was 42% as against 56.7% for all cases. The difference is of doubtful significance. Therefore, there would not appear to be a dramatic fall in the fertility of treatable women after the age of 35. While this latter series is but small it does suggest that the acknowledged fall in fertility associated with a higher age at marriage may not be proportional to irreversible female infertility factors. I want to stress the qualifying term 'irreversible'; for the relatively high conception rate in over thirties is largely a reward for the attention A.I.D. cases receive and which includes not only measures directed to eliminate demonstrable infertility factors but also hormonal support given routinely. In this latter respect I am carrying out the advice of Mr. Christie Brown who has found it useful in his own work (personal communication).

The analysis of conception rates was carried a step further by comparing those cases who were presumed fertile in view of the initial examination with those who required treatment preparatory to A.I.D.

TABLE II

	Sample A %	*Sample B* %
Overall conception rate	54	57.6
Overall failure rate	46	42.3
Conception rate in stigma free cases		67.7
Failure rate in stigma free cases		32.3
Conception rate in stigmatized cases		48.5
Failure rate in stigmatized cases		51.5

Table II shows that in two recent samples covering 124 cases 67.7% of the initially fecund women conceived as against 48.5% of the group requiring treatment. Although this difference is likely to be significant, the failure rate is of greater interest. The overall failure rate is 42.3% and the minimum failure rate 32.3%. Since A.I.D. is only undertaken after elimination of detectable bars to conception, it is reasonable to

assume that the failure rate reflects the incidence of female infertility not detectable by available diagnostic methods. It is humbling to realize that one cannot at present offer any rational treatment to many sterile women.

The incidence of abortion in A.I.D. cases was compared with that in women who conceived by their husbands after treatment of either one or both partners. Male fertility varied of course and the group includes a high proportion of subfecund males. It was found that of 265 successive conceptions by A.I.D. sixty terminated in abortion — a frequency of 22.6%. In 225 contemporary cases of marital conception abortion occurred in 43, i.e. 19.2%. Thus there was no real difference between the two groups. This observation does not exclude the possibility of abortion caused by or contributed to by semen-borne factors; but it suggests that in clinical material of the present type abortion reflects primarily maternal factors. In the 490 cases under discussion there was not a single case of habitual abortion.

Lastly, a remark concerning the incidence of secondary sterility may be added. Many women who have had an A.I.D. child apply in due course for another chance, some as late as five years after their first treatment. None are accepted without a complete re-examination. In a high proportion of these cases infertility factors were detected. This applies both to women who had been free of infertility stigmata and to those who required treatment before conceiving the first time. The commonest acquired secondary infertility factor is represented by cervical disorders complicated by anatomical lesions such as tears and ectropion. About one-third of these women do not conceive again, many others take much longer to become pregnant the second time. Taking a sample group of 15 women seen recently 5 (33%) failed to conceive, and 10 (67%) succeeded. But the mean number of cycles under A.I.D. required for the first conception was 3.1, and for the second conception 12.6. This latter average does not of course include the 5 cases of failure. Previous data rule out the simple explanation of fecundity having fallen through age, and the decline may well reflect fertility hazards associated with pregnancy and childbirth.

SUMMARY

(1) The preliminary investigation of women applying for A.I.D. reveals a 75% incidence of unsuspected infecundity. Since these subjects are not selected except by the known sterility of the husbands their infecundity reflects that of nulligravidae of a corresponding age group selected at random.

(2) In those classed as fecund the conception rate is considerably higher (67.7%) than in those who required preliminary treatment

(48.5%). The failure rate overall is 42.3% even though A.I.D. is only carried out in the absence of, or after elimination of, detectable bars to conception. This failure rate reflects the incidence of female infertility not detectable by available diagnostic methods.

(3) In A.I.D. cases the miscarriage rate is of the same order as that in comparable marital conceptions, 22.6% and 19.2% respectively.

(4) There is no evidence that given adequate attention conception is less likely in the women over thirty years of age than in those under thirty.